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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/714,580	11/14/2003	Paul Wentworth	TSRI 784 5	1792

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THE SCRIPPS RESEARCH INSTITUTE
OFFICE OF PATENT COUNSEL, TPC-8
10550 NORTH TORREY PINES ROAD
LA JOLLA, CA 92037

EXAMINER	
HINES, JANA A	
ART UNIT	**PAPER NUMBER**
1645	
MAIL DATE	**DELIVERY MODE**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/714,580	WENTWORTH ET AL.	
	Examiner	Art Unit	
	JaNa Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-42,44,45 and 48-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-42,44,45 and 48-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. The amendment entered September 2, 2008 has been entered. Claims 40, 48, and 54 have been amended. Claims 1-39, 43 and 46-47 are cancelled. Claims 40-42, 44-45, and 48-58 are under consideration in this office action.

Withdrawal of Rejections

2. The following rejections have been withdrawn in view of applicants' amendments to the claims:

a) The rejection of claims 40-42, and 54-56 under 35 U.S.C. 102(b) as being anticipated by Devanathan et al;

b) The rejection of claims 40-42, 44-45 and 54-58 under 35 U.S.C. 102(b) as being anticipated by Wentworth et al., in light of the Scripps Press Release of November 14, 2002; and

c) The rejection of claims 40, 48 and 54 under 35 U.S.C. 112, second paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 48-51 are rejected under 35 U.S.C. 102(b) as being anticipated by Devanathan et al.

The claims are drawn to a method of generating a ozone to inhibit the growth of a bacterium comprising contacting the bacterium with (i) an antibody that can bind to the bacterium and (ii) a source of singlet oxygen to thereby generate ozone to inhibit the growth of the bacteria, wherein the source of the singlet oxygen would not, on its own, inhibit the growth of the bacterium when exposed to light. The dependant claims are drawn to specific sources for the singlet oxygen and the attachment of the antibody to the sensitizer molecule.

Devanathan et al., teach readily available fluorescein isothiocyante-conjugated antibodies which can be easily converted into targeted agents for antibacterial therapy. Devanathan et al., teach that for photodynamic killing of microorganism, light, oxygen and absorbing dyes called photodynamic sensitizers are essential (page 2980). In an attempt to direct the sensitizer to the target, one can use antibody-photodynamic sensitizer conjugates (page 2980). These have been useful as therapeutic agents for the selective destruction of microorganisms wherein the photodynamic sensitizer must not only be phototoxic, but also selective (page 2980). Devanathan et al., teach disclose that the more halogenated fluorescein rings are, the more efficient photodynamic sensitizers they become (page 2980). Devanathan et al., teach that Rose Bengal is one of these more efficient photodynamic sensitizers (page 2980). Devanathan et al., teach activating the photosensitizing activity of a fluoresceinated antibody that binds to rabbit IgG antibodies (page 2980). The mixing of this diiodofluorescein photodynamic

sensitizer-antibody conjugate with rabbit *anti-Escherichia coli* IgG antibody and illuminating in a mixture of *E. coil* and *Salmonella typhimurium* results in the selective inactivation of the *E. coli* bacteria (page 2980). Similar selectivity is observed with Rose Bengal-sensitized inactivation of strains of *S. typhimurium* (page 2983). The photoactive diiodofluorescein generates singlet oxygen when illuminated and the singlet oxygen is a potent cytotoxicant to *Salmonella* and *E. coil* (page 2983). Devanathan et al., teach that the diiodofluorescein-antibody inactivates the bacteria by the generation of the cytotoxic singlet oxygen (page 2983).

Therefore, Devanathan et al., teach the instant claims.

Response to Arguments

4. Applicant's arguments filed September 2, 2008 have been fully considered but they are not persuasive.

5. The rejection of claims 48-51 under 35 U.S.C. 102(b) as being anticipated by Devanathan et al., is maintained for reasons already of record.

Applicants' urge that Devanathan et al., do not teach that the source of singlet oxygen would not on its own inhibit the growth of the bacteria. However it is the examiner's position that Devanathan is not limited by its teaching of photodynamic sensitizers. Devanathan et al., teach that for photodynamic killing of microorganism, the combination of light, oxygen and absorbing dyes called photodynamic sensitizers are

essential. Therefore a combination of factors and reagents are needed to inhibit the growth of bacteria; thus the source of singlet oxygen, being the photodynamic sensitizer would not, on its own, inhibit the growth of bacteria contrary to applicants' statement. Accordingly, applicants' argument is not persuasive and the rejection is maintained.

Claim Rejections - 35 USC § 102

6. Claims 48-53 are rejected under 35 U.S.C. 102(b) as being anticipated by Wentworth et al., in light of the Scripps Press Release of November 14, 2002.

The claims are drawn to a method of generating a ozone to inhibit the growth of a bacterium comprising contacting the bacterium with (i) an antibody that can bind to the bacterium and (ii) a source of singlet oxygen to thereby generate ozone to inhibit the growth of the bacteria, wherein the source of the singlet oxygen would not, on its own, inhibit the growth of the bacterium when exposed to light. The dependant claims are drawn to specific sources for the singlet oxygen and the attachment of the antibody to the sensitizer molecule.

Wentworth et al., (PNAS, 2000) teach antibodies have the intrinsic capacity to destroy antigens. Antibodies are remarkably adaptable molecules and are known for targeting and effector functions used by vertebrates a defense against foreign invaders (page 10,930). Antibodies are also capable of simply binding and more complex chemical reactions (page 10,930). Antibodies have the capacity to convert molecular oxygen into hydrogen peroxide, thereby effectively linking recognition and killing events

(page 10,930). Wentworth et al., disclosed this capability with whole antibodies and $F(ab')_2$ fragments (see the materials and methods section). The sensitization and quenching assays teach a solution of horse IgG antibody and sensitizer molecule, hematopophyrin were placed in proximity to a strip of light and the concentration of hydrogen peroxide produced was determined (page 10,930). Wentworth et al., teach that superoxide anion radicals are the direct precursor of hydrogen peroxide and the toxic derivatives it spawns, such as hydroxyl radials (HO*). Thus Wentworth et al., teach that the reactive oxygen species generated is a superoxide radical, hydroxyl radical or hydrogen peroxide. It is noted that the art is silent with respect to the generation of an ozone as a reactive oxygen species.

It is noted that the Scripps Press Release inherently teaches the production of ozone by antibodies during bacterial killing has played an hitherto unknown role in immune protection (Scripps Press Release). The ozone is part of a previously unrecognized killing mechanism that enhances the defensive role of antibodies by allowing them to subject pathogens to hydrogen peroxide and participate directly in their killing. Antibodies produce the chemical oxidant hydrogen peroxide which is lethal to bacterial cells because it pokes holes in their cell walls, bursting the cells and killing them. The antibodies reduce singlet oxygen and produce ozone as a side product. The authors state that all antibodies have the ability to do this. Therefore the generation of hydrogen peroxide and ozone as a side product, are inherent abilities that antibodies have. Thus, the Scripps Press Release teaches that inherently, antibodies will

generate ozone as a reactive species which will inhibit the growth of a bacterial microbe.

Therefore Wentworth et al., in light of the Scripps Press Release teach the instant claims.

Response to Arguments

7. The rejection of claims 48-53 under 35 U.S.C. 102(b) as being anticipated by Wentworth et al., in light of the Scripps Press Release of November 14, 2002 is maintained.

Applicants' argue that the antibodies are will not bind the bacterium. However, the art teaches that antibodies have the intrinsic capacity to destroy antigens because they are known for targeting and binding foreign invaders, such as bacteria. Therefore applicants' assertion is not persuasive, because it is well known in the art for antibodies to bind bacteria. Therefore the rejection is maintained.

Claim Rejections - 35 USC § 102

8. Claims 48-51 are rejected under 35 U.S.C. 102(b) as being anticipated by Berthlaume et al.

The claims are drawn to a method of generating a ozone to inhibit the growth of a bacterium comprising contacting the bacterium with (i) an antibody that can bind to the bacterium and (ii) a source of singlet oxygen to thereby generate ozone to inhibit the

growth of the bacteria, wherein the source of the singlet oxygen would not, on its own, inhibit the growth of the bacterium when exposed to light. The dependant claims are drawn to specific sources for the singlet oxygen and the attachment of the antibody to the sensitizer molecule.

Berthlaume et al., teach antibody-targeted photolysis of bacteria *in vivo.* Berthlaume et al., teach an antibody-targeted photolysis method which uses antibody bound photosensitizers which are toxic only upon activation of light (page 703). Berthlaume et al., teach that bacterial killing *in vitro* using tin (IV) chlorine e6 as the photosensitizer was shown to be highly efficient in the production of singlet oxygen and other short-lived species (page 703). The results of this study show that specific tin (IV) chlorine e6-monoclonal antibody conjugates directed against *P. aeruginosa* can specifically kill more than 75% of the bacteria (page 703). Berthlaume et al., teach transport studies of antibody fragments have shown improved and rapid infiltration of the selected target sites (page 705).

Therefore, Berthlaume et al., teach the instant claims.

Response to Arguments

9. The rejection of claims 48-51 under 35 U.S.C. 102(b) as being anticipated by Berthlaume et al., is maintained for reasons already of record.

Applicants' urge that Berthlaume et al., does not teach that the source of singlet oxygen would not on its own inhibit the growth of the bacteria. Berthlaume et al., teach

that for photodynamic killing of microorganism, the combination of light, oxygen and photodynamic sensitizers are essential. Therefore a combination of factors and reagents are needed to inhibit the growth of bacteria; thus the source of singlet oxygen, would not, on its own, inhibit the growth of bacteria. Accordingly, Berthlaume et al., meets the limitations of the claims; applicants' argument is not persuasive; thus the rejection is maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. The new matter rejection of claims 40-42, 44, 45 and 54-58 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained.

The rejection was on the grounds that neither the specification nor originally presented claims provides support for a method of generating a reactive oxygen species to inhibit the growth of a bacterium comprising contacting the bacterium with (i) an antibody or antibody fragment that can bind to the bacterium and (ii) a source of

singlet oxygen wherein the source of singlet oxygen is not conjugated to the antibody or another molecule.

Applicant did not point to support in the specification for the instantly claimed method with respect to the recitation “or another molecule”. Since the only disclosure teachings about the source of singlet oxygen being "conjugated" to anything were in the context of its being "conjugated to the antibody" (e.g. page 78, lines 1-4; page 83, lines 11-18; and page 93, lines 17-24) it constitutes new matter for applicant to recite that the source of singlet oxygen being "is not conjugated" to "another molecule". The mere absence of a positive recitation (i.e. of another molecule, to which the source of singlet oxygen could be conjugated) is not a basis for an exclusion. See MPEP 2173.05(i).

Therefore the rejection is maintained contrary to applicants’ arguments.

Conclusion

12. No claims allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached Monday thru Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Robert Mondesi, can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/JaNa Hines/
Examiner, Art Unit 1645

/Mark Navarro/
Primary Examiner, Art Unit 1645